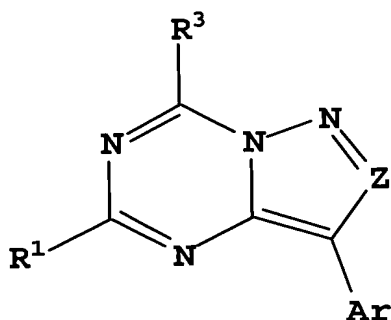
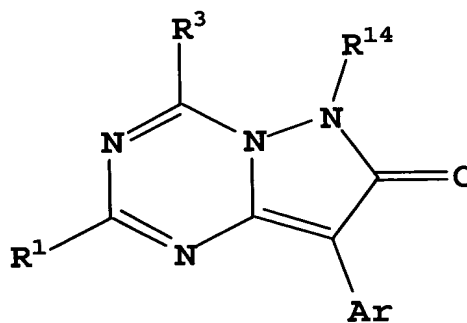


B¹ 1. A method of treating a disorder induced or facilitated by CRF in a mammal comprising administering to said mammal a therapeutically effective amount of a compound of Formulae (1) or (2):



(1)



(2)

isomers thereof, stereoisomeric forms thereof, mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt forms thereof, wherein:

Z is CR²;

Ar is selected from phenyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, furanyl, thienyl, benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each Ar optionally substituted with 1 to 5 R⁴ groups and each Ar is attached to an unsaturated carbon atom;

R¹ is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl, C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;

R³ is selected from:

-H, SH, S(O)_nR¹³, COR⁷, CO₂R⁷, OC(O)R¹³, NR⁸COR⁷, N(COR⁷)₂,

contd.
B¹

NR⁸CONR⁶R⁷, NR⁸CO₂R¹³, N(OR⁷)R⁶, CONR⁶R⁷, aryl, heteroaryl and heterocycle, or
-C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₄-C₁₂ cycloalkylalkyl or C₆-C₁₀ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl and heterocyclyl;

R⁴ is independently selected at each occurrence from: C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷, or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷, or S(O)_nR⁷;

R⁶, R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:

-H,
-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl,
-aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups;

contd.
B1
R⁸ is independently selected at each occurrence from H or C₁-C₄ alkyl;

R⁹ and R¹⁰ are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;

R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl, or C₃-C₆ cycloalkyl;

R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-, heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

R¹⁴ is selected from C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₃-C₈ cycloalkyl, or C₄-C₁₂ cycloalkylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, and C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl and C₁-C₆ alkylsulfonyl;

R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;

aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵,

CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵; and

n is independently at each occurrence 0, 1 or 2.

REMARKS

Reconsideration of the present application is respectfully requested in view of the amendment to the claims and the following comments.

Claims 1, 2, 37 and 38 are pending in the application. Claim 1 has been amended to clarify the definition for the R⁶, R⁷, R^{6a}, and R^{7a} substituents. This definition has not been substantively amended, but merely re-typed for purposes of clarification.

Claims 1, 2, 37 and 38 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that the re-typed definition for the R⁶, R⁷, R^{6a}, and R^{7a} substituents in Claim 1 clarifies that no text was omitted, and that the claims are thus not indefinite. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 1, 2, 37 and 38 also stand rejected under 35 U.S.C. § 112, first paragraph, because Claim 1 does not include certain provisos that are set forth on pages 25 to 26 of the specification. Accordingly, the Examiner has asserted that Claim 1, without the provisos, is not supported in the specification. Applicants respectfully traverse this rejection.

Applicants respectfully submit that Claim 1, as currently pending is fully supported by the specification, for example, at pages 14 to 20. Applicants note that the genus of